The spectrum of haemodynamic support in cardiogenic shock: how to choose and use

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INTRODUCTION

Cardiogenic shock is still the most important prognostic factor for short-term mortality in acute coronary syndromes, with mortality rates approaching 50% at 30 days [1, 2]. Haemodynamic support can be achieved by inotropics and/or vasopressors as well as mechanical means such as intra-aortic balloon pumping (IABP) or percutaneous implantable left ventricular assist devices (LVAD) or complete extra-corporeal life support (ECLS) with extra-corporeal membrane oxygenation (ECMO) [3]. A schematic illustration of the different systems can be found in Figure 1. Currently there is only limited data derived from randomised trials evaluating the different percutaneous support systems. Thus, many guideline recommendations are expert recommendations with a scientific level of evidence grade C [4, 5]. In addition, the cardiogenic shock recommendations in current guidelines are relatively short, dealing mainly with interventional treatment in an acute setting. Therefore, recently dedicated guidelines for cardiogenic shock in acute myocardial infarction have been published for Germany and Austria dealing also with all aspects of intensive care treatment [6].

MECHANICAL HAEMODYNAMIC SUPPORT: DIFFERENT SYSTEMS

Mechanical support can be achieved either with active continuous flow systems such as axial flow devices, left atrial-to-femoral artery continuous flow devices, ECLS or a reduction in cardiac afterload by IABP.

Intraaortic balloon counterpulsation

IABP is a mature technique which has been widely used for support in cardiogenic shock since its first use in the 1960s [7]. The IABP, a balloon mounted on a vascular catheter, is inserted via the femoral artery and placed in the descending aorta directly distal to the origin of the left subclavian artery. The balloon is inflated during diastole and deflated in the systolic phase of the cardiac cycle. Modern systems have automated settings and small catheter diameter, therefore handling is easier and fewer vascular complications occur. Until recently, only registry data existed supporting a favourable outcome with IABP in acute myocardial infarction complicated by cardiogenic shock without revascularisation or after thrombolysis. In the European and American guidelines until 2012, IABP support in cardiogenic shock was a Class I indication [8, 9]. A meta-analysis on registry data — due to the lack of randomised trials — published in 2009 challenged these recommendations, showing higher mortality in patients after primary percutaneous coronary intervention (PCI) in cardiogenic shock [10]. Therefore, in the actual IABP support in cardiogenic shock was downgraded to a Class IIb recommendation in European and Class IIa recommendation in American guidelines [4, 5]. In addition, the large-scale randomised IABP-SHOCK II trial showed no benefit for IABP support in cardiogenic shock complicating myocardial infarction after early revascularisation [11, 12]. This study included 600 patients in 37 German centres randomised either to IABP or no IABP in addition to early revascularisation and optimal intensive care treatment. No differences were observed in the primary endpoint 30-day mortality or in secondary endpoints or any analysed subgroups. Patients with mechanical complications such as ventricular septal defects or acute mitral regurgitation due to papillary muscle rupture were excluded from this trial. In these patients, an IABP implantation may be still considered based on haemodynamic benefits [13]. For the group of patients needing emergency surgical revascularisation due to extended coronary artery disease, there is only limited data. With only six patients (three in each group) undergoing immediate coronary artery bypass grafting in IABP-SHOCK II, no reasonable analysis is possible. There is a lack of any randomised data in this setting. However,

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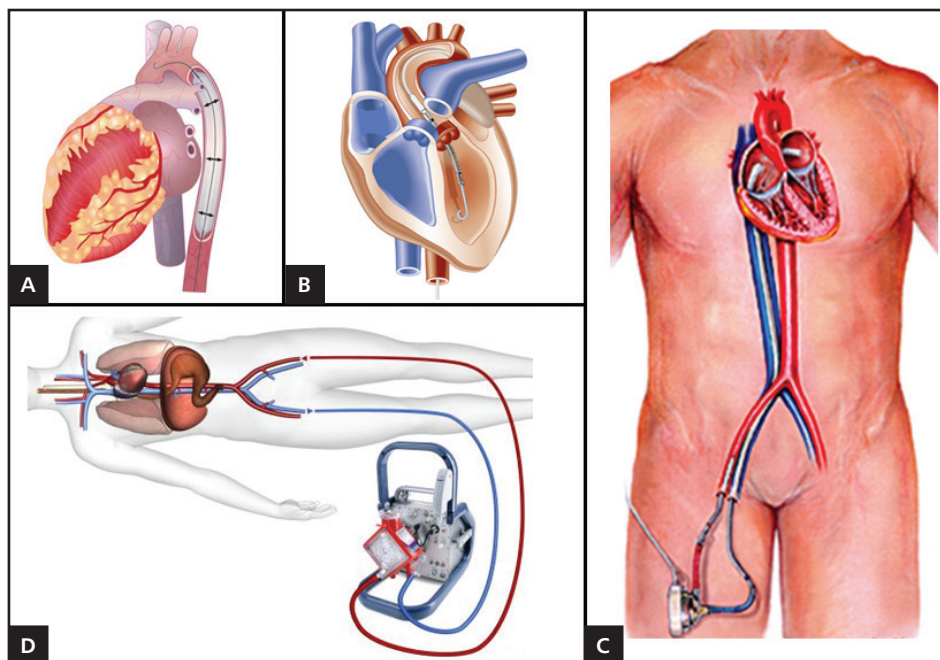
Figure 1. Overview of the different devices for percutaneous haemodynamic support; **A**. Intra-aortic balloon pumping; **B**. Impella® 2.5; **C**. TandemHeart™; **D**. Extra-corporeal membrane oxygenation

any difference in outcome based on the type of reperfusion is pathophysiologically implausible.

Percutaneous left ventricular assist devices

In the last decade, new systems for active left ventricular support designed for percutaneous insertion have been developed. An overview of the actual available systems is given in Table 1. These systems can be differentiated into active systems with or without the additional possibility of oxygenation and decarboxylation.

Extra-corporeal life support

Systems with the possibility of lung assist are summarised under the term ECLS or the older name ECMO. These systems are more or less developments of conventional heart-lung machines. The newest generations of these systems are developed for percutaneous insertion and also miniaturised to make transportation possible [14]. Two newer systems are dedicated to allow transportation of patients on ECLS. These systems are the Lifebridge® (Lifebridge Medizintechnik AG, Ampfing, Germany) and the CardioHelp® (Maquet Cardiopulmonary AG, Hirrlingen, Germany). The ECLS is inserted via the transfemoral approach with a 16–19 French arterial cannula reaching the descending aorta and a long 18–21 French venous cannula which is advanced from the femoral vein into the right atrium. The blood coming from the right atrium is accelerated by a centrifugal pump and runs through a membrane oxygenator back to the iliac artery (Fig. 2). These systems can establish a flow up to 7 L/min and

can also completely replace the lungs. First line complications with ECLS occur due to the large cannula size at the insertion site with predominant bleeding or lower limb ischaemia. To avoid the latter, an antegrade sheath can be inserted to maintain adequate perfusion of the leg with the arterial cannula. Although insertion of the cannula is relatively easy and can be performed without a cardiac operation room setting, a perfusionist is often needed to set up the machines and prime the lines. Also nurses and treating physicians on the intensive care unit have to be familiar with the system to recognise and handle potential problems and complications. This makes the systems impractical for smaller hospitals. However, in some tertiary care centres, special teams have been established to travel to referring hospitals with the complete equipment to implant an ECLS in unstable patients for stabilisation and to transfer them on haemodynamic support to a dedicated tertiary care centre for further care [14–16].

TandemHeart™

An active LVAD without oxygenation is the TandemHeart™ (Cardiac Assist, Inc, Pittsburgh, PA, USA). Oxygenated blood is removed by a left atrial cannula which is placed via the transseptal approach from the femoral vein. The blood is then returned after acceleration with a centrifugal pump through an arterial cannula in the femoral artery. With the TandemHeart™ a flow of up to 4 L/min can be achieved; detailed specifications are given in Table 1. Like all active systems, anticoagulation is needed which is maintained by continuous heparin infusion. As regards the efficacy of this system, only two small

Table 1. Technical features of currently available percutaneous left ventricular assist devices for haemodynamic support

	IABP	Tandem Heart™	Impella Recover® LP 5.0	Impella Recover® LP 2.5	Impella CP®	ECLS (multiple systems)
Catheter size [French]	7–8 (sheathless insertion possible)	–	9	9	9	
Cannula size [French]	–	21 venous, 12–19 arterial	21	12		17–21 venous, 16–19 arterial
Flow [l/min]	0	Max. 4.0	Max. 5.0	Max. 2.5	3.7 – 4.0	Max. 7.0
Pump speed [rpm]	0	Max. 7,500	Max. 33,000	Max. 51,000	Max. 51,000	Max. 5,000
Insertion/placement	Percutaneous (femoral artery)	Percutaneous (femoral artery + left atrium after transseptal puncture)	Peripheral surgical cutdown (femoral artery)	Percutaneous (femoral artery)	Percutaneous (femoral artery)	Percutaneous (femoral artery and vein)
Anticoagulation	+/–	+	+	+	+	+
Recommended duration of use	–30 days (no upper limit)	–14 days	10 days	10 days	10 days	–7 days
CE-certification	+	+	+	+	+	+
FDA	+	+	+	+	–	+
Relative costs compared to IABP	–	+++++	++++	+++	+++	++ Depending on system

CE — conformité européenne; FDA — Food and Drug Administration; IABP — intra-aortic balloon pump; ECLS — extra-corporeal life support

trials have found better haemodynamic parameters with LVAD compared to IABP. However, due the small sample size, there is currently no randomised evidence of a survival benefit [17, 18]. In a recent single-centre observational study in severe refractory cardiogenic shock with 47% of the patients under active cardiopulmonary resuscitation, the TandemHeart™ was used as a bailout device. In this patient cohort, haemodynamic parameters improved significantly and the reported mortality rates (40.2% at 30 days and 45.3% at six months) were lower than anticipated in light of the severity of haemodynamic compromise [19]. However, the major limitation is that this was only a registry trial.

The TandemHeart™ is mainly suitable for patients with left ventricular dysfunction, although its use in right ventricular failure has also been described [20, 21]. Due to its mode of action, this system may not be the correct choice in patients with coexisting acute pulmonary problems. Contraindications are severe aortic regurgitation and significant peripheral artery disease; a distal aortography with visualisation of the iliac arteries is often recommended before implantation. In addition, relatively good experience in performing transseptal punctures is needed.

Impella®
Another percutaneous system is the Impella® (Abiomed Europe, Aachen, Germany), an LVAD with axial flow. This pump is available in different sizes. The Impella® 2.5 (flow rate up to 2.5 L/min) is placed percutaneously, and the Impella® 5.0 (flow rate up to 5.0 L/min) by surgical cutdown, both via the femoral artery. A new system with a flow rate up to 4.0 L/min, the Impella® CP, was CE marked in the European Union in April 2012 and is also implanted percutaneously via the femoral artery. This system has a mounted pigtail-catheter at its tip which is placed via the aortic valve in the left ventricle. A microaxial pump with rotation rates up to 50,000 rpm delivers the blood from the left ventricle through the catheter to the ascending aorta.

This concept can provide better left ventricular unloading than support with ECLS [22]. However, randomised data on the Impella® is limited. A small study comparing it to IABP showed better haemodynamic support, but with only 25 patients included, this trial was underpowered for any conclusions on outcome [23]. A planned large-scale study, the RECOVER II trial (www.clinicaltrials.gov: NCT00972270), was stopped early because of low inclusion rate and funding problems. A recent cohort study showed similar outcomes in post resuscitation cardiogenic shock patients with the Impella® compared to IABP, concluding that this concept may be feasible. However, there was a trend towards higher bleeding rates in the Impella® group [24]. The observed bleeding rates in this study were similar to findings in the Impella-EUROSHOCK-registry [25]. A concept to combine the
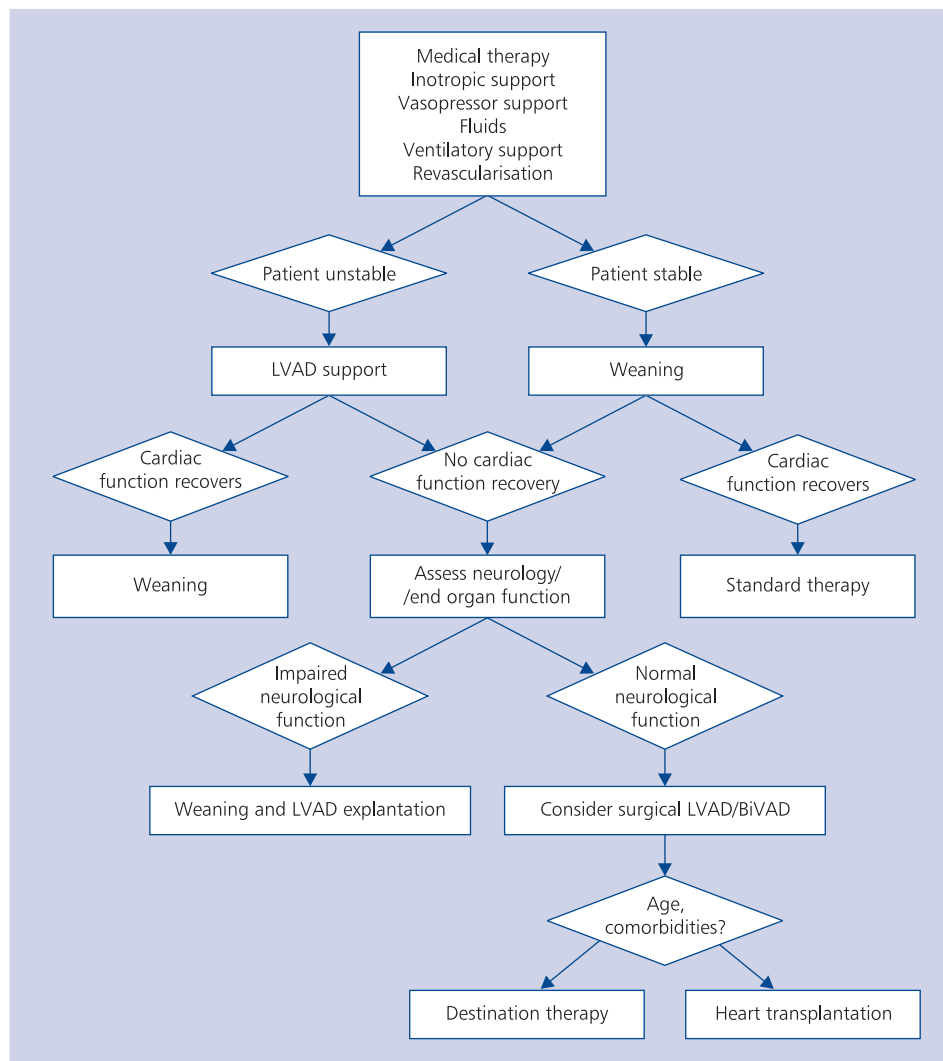
Figure 2. Possible treatment algorithm in cardiogenic shock; LVAD — left ventricular assist device; BiVAD — biventricular assist device

benefits of the Impella® with the possibility for oxygenation with ECLS was described recently in some case series [26–28]. This concept may be plausible for haemodynamic purposes, but the combination may even result in more bleeding complications. Therefore, this concept needs further randomised evaluation before a recommendation for combination of ECLS and Impella® can be given. For right heart failure, a dedicated system known as the Impella® RD is available, but evidence in the literature is limited to a few case series [29–31].

INDICATIONS AND CHOICE OF SYSTEM
Timing of implantation
In infarct related cardiogenic shock, initial haemodynamic stabilisation after revascularisation by primary PCI should be managed with fluids and catecholamines [3]. Based on a meta-analysis by Cheng et al. [32] showing no benefit over IABP with more complications in the LVAD treated patients, first-line treatment with active LVAD is currently a Class III

recommendation. Therefore, European and American guidelines both categorise the use of active LVAD in refractory cardiogenic shock after myocardial infarction as a Class IIb indication with a level of evidence C [4, 5]. The IABP still has a Class IIa (American guideline) and Class IIb (European guideline) recommendation, with a level of evidence B. However, these recommendations do not take into account the published IABP-SHOCK II trial which is the only adequately powered randomised trial in this setting. Based on the IABP-SHOCK II trial which was published one day after the European guideline release, IABP cannot be recommended in general [12, 33]. As shown in IABP-SHOCK II, approximately 60% of patients will recover to haemodynamic stability without any additional active support. In these patients, LVADs may even cause harm due to their inherent complications. There might also be a patient cohort where any treatment might be futile. On the other hand, in a selected group of patients with refractory cardiogenic shock, LVAD treatment may be the only option

for survival. Currently, the selection of patients and timing of implantation is not well defined and mainly based on personal experience and/or institutional recommendations that are not based on evidence-based trials. A scoring system to predict prognosis of these patients needs to be established but is currently still lacking. To date serum lactate and/or its clearance as well as the possibility of weaning catecholamine support may be the best indicators [34, 35], In septic shock, a randomised trial in 300 patients comparing serum lactate clearance vs. central venous oxygen saturation for treatment guidance designed for non-inferiority met the primary endpoint, with in-hospital mortality rates of 25% vs. 34% [36]. Another registry trial found that lactate clearance may be even better in prognosis prediction than central venous oxygen saturation [37]. For cardiogenic shock, only one small study has focused on serum lactate clearance, showing similar results [38]. Larger trials are warranted to confirm the finding of serum lactate clearance for sepsis in cardiogenic shock.

Choice of device

There have been no comparative trials showing any benefit of one active device over the other. Therefore, all decisions for device selection are based only on pathophysiological, haemodynamic and clinical considerations. There is also no data on how much support is necessary for the failing heart in cardiogenic shock; this is particularly relevant for the Impella® 2.5 which might not be able to provide sufficient haemodynamic support. In patients with primary left ventricular failure and no relevant concomitant pulmonary problems, the TandemHeart™ and the Impella® may be useful. For biventricular or respiratory failure, a complete ECLS would be the better choice [39]. In general, familiarity with the device of the implanting cardiologist, as well as the team on the intensive care unit, is usually more important than theoretical advantages of one device over another. This ensures optimal device management and also the better handling of any potential complication.

Another important issue is the treatment of weaning failure after percutaneous LVAD implantation. In general, these devices are inserted as bridge-to-recovery, bridge-to-transplant, or as bridge-to-surgical LVAD. In cases where none of the above described options is achievable, any implantation of an active assist device should be considered futile. However, often the clinical situation is unclear. Therefore, in patients with equivocal neurology, haemodynamic stabilisation with a percutaneous LVAD may be instituted to allow subsequent halt of the sedation to assess neurologic function for further therapeutic decision making. To optimise secondary care for this very sick patient group, further treatment should always be maintained by highly experienced tertiary care centres with the possibility of cardiac and lung transplantation and a permanent assist device programme. A potential treatment algorithm with a stepwise approach for escalation of haemodynamic support is shown in Figure 2.

CONCLUSIONS

The use of active LVAD support in cardiogenic shock has grown significantly in recent years. Since IABP has not been able to prove its benefit in these patients, active LVAD may reflect a treatment option in refractory cardiogenic shock. The haemodynamic benefit has been proven but outcome data is lacking and there is an increase in complications of these highly invasive devices. Clear algorithms and scores for timing and indication of LVAD are missing. They need to be established and validated in future trials.

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